CLAIMS

What is claimed is:

1. A Synthetic nuclease resistant antisense oligodeoxynucleotides having a nucleotide sequence selected from the group consisting of SEQ ID No:4 and SEQ ID No:6.

- 2. The synthetic nuclease resistant antisense oligodeoxynucleotides as set forth in claim 1 having phosphorothicate bonds linking between the four 3'-terminus nucleotide bases for providing nuclease resistance.
- 3. A pharmaceutical or medical composition comprising as active ingredient at least one synthetic nuclease resistant antisense oligodeoxynucleotide as set forth in claim 1 in a physiologically acceptable carrier or diluent.
- 4. The pharmaceutical composition as set forth in claim 1 comprising either SEQ ID No.4 or SEQ ID No.6 and at least one other non-control AS-ODN selected from Tables 1 and 2 wherein the percent inhibition is greater than 25%.

5. A synthetic nuclease resistant antisense oligodeoxynucleotide capable of selectively modulating human tumor necrosis factor alpha by targeting exon sequences flanking donor splice sites thereby regulating expression of TNF-α.

6. The synthetic nuclease resistant antisense oligodeoxynucleotides having a nucleotide sequence as set forth in claim 5 selected from the group consisting of SEQ ID No:4 and SEQ ID No:6.

R. A pharmaceutical composition for selectively modulating mammalian tunor necrosis factor alpha in a mammal in need of such treatment consisting of an effective amount of at least one active ingredient as set forth in claim 1 and a pharmaceutically physiologically acceptable carrier or diluent.

8. A pharmaceutical or medical composition comprising as active ingredient at least one synthetic nuclease resistant antisense oligodeoxynucleotides as set forth in claim 6 in a physiologically acceptable carrier or diluent.

B

9. A pharmaceutical composition for modulating human tumor necrosis factor alpha in a patient in need of such treatment consisting of

an effective amount of at least one active ingredient as set forth in claim 6 or a ribezyme comprising a sequence complementary to at least a portion of exon sequences flanking donor splice sites in $TNF-\alpha$; and

a pharmaceutically physiologically acceptable carrier or diluent.

- 10. A method of modulating expression of human tumor necrosis factor alpha in a mammal by administering a pharmaceutical composition as set forth in claim 5.
- 11. A DNA expression sequence comprising a transcriptional initiation region and a sequence encoding an oligonucleotide as set forth in claim 5.
- 12. A vector comprising a DNA sequence according to claim 11.

APO AY

and B